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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/404,979	09/22/1999	T. VENKAT GOPAL	GENAPP.002RA	8979

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EXAMINER
MCKELVEY, TERRY ALAN

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 12/17/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/404,979	GOPAL, T. VENKAT	
	Examiner	Art Unit	
	Terry A. McKelvey	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 September 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *22,26* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after allowance or after an Office action under *Ex Parte Quayle*, 25 USPQ 74, 453 O.G. 213 (Comm'r Pat. 1935). Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 9/3/02 has been entered.

Priority

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

> An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)).

The instant application was filed as a reissue of 08/240,514, filed 5/14/94, U.S. Patent No. 5,670,347. This information is required to be in the first sentence of the application.

The Jennings and Wriggers Declarations under 37 CFR 1.132 filed 9/3/02 are insufficient to overcome the rejection of the claims under 35 USC 102(a), 35 USC 102(e), and 35 USC 103(a) as set forth below for the following reasons.

The Declarations attempt to make a distinction between the spacer as described in Woo et al and the hinge region as claimed in the instant application. However, although the two declarations are convincing that some definitions in the art make a distinction between "spacer" and "hinge region", the declarations are not convincing that the hinge region as claimed and more specifically defined by the instant specification corresponds to the definition set forth in the declarations. There is nothing in the instant specification which supports the distinction between spacer and hinge region made by the declaration. As described in detail in the rejections below, the only definition set forth for hinge region in the instant specification corresponds to the structure and function of spacer as argued in the declarations, for a distance holder between the attached moieties or preventing the attached

moieties from coming into contact, i.e., for preventing stearic hindrance, which the specification specifically describes as the function of the hinge region. There is nothing in the definition of hinge region specifically set forth in the instant specification which is directed to allowing a high degree of freedom of movement between the attached moieties. Therefore, based upon the description and definition of the hinge region as set forth in the specification, the Woo et al gly-ser spacer qualifies as a hinge region of neutral amino acids as claimed and thus the claimed invention is anticipated and/or made obvious by the cited references as described in the rejections below.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1-3, 5-6, 8, 10-11, and 14 are rejected under 35 U.S.C. 102(e) as being anticipated by Woo et al (U.S. Patent No. 5,994,109), and, alternatively, as being anticipated by Smith et al (WO 93/18759).

The rejections are based upon essentially the same teachings present in the published international application and the corresponding U.S. patent. For the sake of brevity and clarity, only the identity and location of the teachings of the U.S. patent are referred to in the following rejection. The corresponding teachings are also present in the published international application taught by Smith et al.

Woo et al teach a nucleic acid transporter system (nucleic acid transporter and method of producing a transformed cell) comprising a nucleic acid containing genetic information of interest (such as a DNA structural sequence) noncovalently bound

to a transporter nucleic acid comprising a nucleic acid binding molecule (such as a polymeric chain of basic residues, polylysine for example), a nuclear ligand (NLS), and a spacer (such as a $(gly_{1-6}\text{-}ser_{1-6})_{3-20}$ repeat spacer) between the binding molecule and nuclear ligand (throughout the reference, especially columns 124-126). The gly-ser spacer taught by Woo et al reads on "a hinge region of neutral amino acids" because the specification of the instant application defines the hinge region separating the DNA binding domain and NLS peptide as a "hinge region of neutral amino acid, to minimize stearic interference between the two domains. For this purpose, the hinge region ranges in length from about six to twenty-five amino acids, and contains a stretch of neutral small amino acids without any bulky hydrophobic or ionic side chains." (column 7 of U.S. Patent No. 5,670,347, which is the parent case of the instant case, referred to instead of the identical instant application, for ease of reference). The Woo et al gly-ser spacer has the same structure as that of the instant application's hinge region, consists of 6-240 small neutral amino acids, including having a glycine as a neutral amino acid (and which encompasses the 6-25 range taught by the instant application). The Woo et al spacer has the same function as the instant application's hinge region, to minimize stearic

interference. Therefore, the lys-ser spacer taught by Woo et al reads on the hinge region of the instant application and thus the nucleic acid transporter system containing the gly-ser spacer taught by Woo et al anticipates the claimed transfection vector containing a hinge region of neutral amino acids. Woo et al also teach that the nucleic acid noncovalently bound to the transporter can be any nucleic acid that is desired to be expressed in a cell, such as including oncogenes such as myc (columns 5-6 and 10).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-11 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Woo et al (U.S. Patent No. 5,994,109) or Smith et al (WO 93/18759), in view of Short (U.S. Patent No. 5,589,392).

The rejection is based upon essentially the same teachings present in the published international application and the corresponding U.S. patent. For the sake of brevity and clarity, only the identity and location of the teachings of the U.S. patent are referred to in the following rejection. The corresponding teachings are also present in the published international application taught by Smith et al.

Woo et al teach a nucleic acid transporter system (nucleic acid transporter and method of producing a transformed cell) comprising a nucleic acid containing genetic information of interest (such as a DNA structural sequence) noncovalently bound to a transporter nucleic acid comprising a nucleic acid binding molecule (such as a polymeric chain of basic residues, polylysine for example), a nuclear ligand (NLS), and a spacer (such as a $(gly_{1-6}\text{-}ser_{1-6})_{3-20}$ repeat spacer) between the binding molecule and nuclear ligand (throughout the reference, especially columns 124-126). The gly-ser spacer taught by Woo et al reads on "a hinge region of neutral amino acids" because the specification of the instant application defines the hinge region separating the DNA binding domain and NLS peptide as a "hinge region of neutral amino acid, to minimize stearic interference between the two domains. For this purpose, the hinge region ranges in length from about six to twenty-five

amino acids, and contains a stretch of neutral small amino acids without any bulky hydrophobic or ionic side chains." (column 7 of U.S. Patent No. 5,670,347, which is the parent case of the instant case, referred to instead of the identical instant application, for ease of reference). The Woo et al gly-ser spacer has the same structure as that of the instant application's hinge region, consists of 6-240 small neutral amino acids, including having a glycine as a neutral amino acid (and which encompasses the 6-25 range taught by the instant application). The Woo et al spacer has the same function as the instant application's hinge region, to minimize stearic interference. Therefore, the lys-ser spacer taught by Woo et al reads on the hinge region of the instant application and thus the nucleic acid transporter system containing the gly-ser spacer taught by Woo et al anticipates the claimed transfection vector containing a hinge region of neutral amino acids. Woo et al also teach that the nucleic acid noncovalently bound to the transporter can be any nucleic acid that is desired to be expressed in a cell, such as including oncogenes and transcription factors such as myc, and the use of any vectors, such as viral vectors (columns 5-6 and 10).

Woo et al do not specifically teach that the NLS can be a particular NLS such as the SV40 large T antigen NLS and that the

NLS is located at the amino terminus and the polymeric basic amino acid chain is located at the carboxyl terminus. A vector comprising a gene encoding a SV40 large T antigen and a transcription factor is also not specifically taught.

Short teach the use of a fusion of the SV40 large T antigen NLS to a heterologous sequence, for nuclear localization of the fusion polypeptide. This reference also teaches that although the SV40 large T antigen NLS is exemplary, an NLS from another protein can be used (columns 5-6).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the SV40 large T antigen NLS taught by Short into the nuclear transporter system taught by Woo et al because Short teaches that it is within the ordinary skill in the art to make a fusion between the SV40 large T antigen NLS (or any other NLS) and a heterologous protein and Woo et al teaches the use of a nuclear ligand such as an NLS in the nucleic acid transporter system taught by Woo et al.

One would have been motivated to do so for the expected benefit of using the exemplary SV40 large T antigen taught by Short in the nucleic acid transporter taught by Woo et al. Use of a known product for its known and expected properties is obvious. Based upon the teachings of the cited references, the

high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success in practicing the claimed invention.

Regarding the inclusion of a gene encoding a SV40 large T antigen and a transcription factor, it would have been obvious to include those genes in a nucleic acid vector to be transported because Woo et al teach that any nucleic acids can be transported using the system, such as specific oncogenes and transcription factors and use of viral vectors (which is and was well known in the art to encompass SV40 based vectors that include the gene for large T antigen).

Regarding the NLS being located at the amino terminus and the polymeric basic amino acid chain is located at the carboxyl terminus, it would have been obvious for the nucleic acid transporter made obvious by the combined teachings of the cited references because NLS is present at the amino terminus in proteins normally and as shown by the cited references.

Claims 1-3, 5-6, 8, 10-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Woo et al (U.S. Patent No. 5,994,109) or Smith et al (WO 93/18759), in view of Gorman (U.S. Patent No. 5,024,939).

The teachings of Woo et al/Smith et al are recited above and applied as before. These references do not specifically teach that the DNA sequence to be transported comprises another gene such as a DHFR or a tk gene.

Gorman teaches transfecting into a eukaryotic or mammalian cell an expression vector containing a selectable marker such as DHFR or tk, necessary for survival or growth of the cell transformed with the vector (column 7). This reference also teaches the use of the selectable marker containing vector to select for vector transformed cells (column 7).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to include a selectable marker gene such as DHFR or tk as taught by Gorman in the nucleic acid to be transported in the nucleic acid transporter taught by Woo et al/Smith et al because Gorman teaches that it is within the ordinary skill in the art to include DHFR or tk in a nucleic acid vector to be transported into cells and Woo et al/Smith et al teach a nucleic acid vector to be transported into cells.

One would have been motivated to do so for the expected benefit of being able to select for cells that are transformed with the nucleic acid transporter system taught by Woo et al/Smith et al using the selection system taught by Gorman.

Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success in practicing the claimed invention.

Amending the claimed invention to add the limitation that the hinge region consists of amino acids selected from the group consisting of glycine, alanine, leucine, and isoleucine, would be remedial in overcoming the art rejections of record.

Conclusion

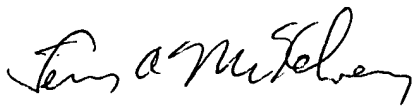
No claims are allowed.

Certain papers related to this application may be submitted to Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone numbers for the Group are (703) 308-4242 and (703) 305-3014. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning rejections or other major issues in this communication or earlier communications from the examiner should be directed to Terry A. McKelvey whose telephone number is (703) 305-7213. The examiner can normally be reached on Monday through Friday, except for Wednesdays, from about 7:30 AM to about 6:00 PM. A phone message left at this number will be responded to as soon as possible (i.e., shortly after the examiner returns to his office).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel, can be reached at (703) 305-1998.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.



Terry A. McKelvey, Ph.D.
Primary Examiner
Art Unit 1636

December 16, 2002